Citation:

McLaughlin T, Carter S, Lamendola C, Abbasi F, Yee G, Schaaf P, Basina M, Reaven G. Effects of moderate variations in macronutrient composition on weight loss and reduction in cardiovascular disease risk in obese, insulin-resistant adults. *Am J Clin Nutr.* 2006 Oct;84(4):813-21.

PubMed ID: 17023708

Study Design:

Randomized Clinical Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To evaluate the effect of moderate variations in carbohydrate and fat content of calorie-restricted diets on the ability to lose weight and on the associated changes in cardiovascular disease (CVD) risk factors in obese, insulin-resistant persons.

Inclusion Criteria:

- Body mass index between 29 and 36 kg/m²
- No history of weight loss in the past 3 months
- No use of weight loss drugs
- No history of major organ disease
- Those who met study criteria for insulin-resistance after taking an insulin suppression test.

Exclusion Criteria:

- Those with clinical or laboratory evidence of anemia, kidney or liver disease, or diabetes mellitus.
- Those who did not meet the study's definition of insulin-resistance after taking an insulin suppression test.

Description of Study Protocol:

Recruitment: Participants were recruited by newspaper articles and advertisements.

Design: Randomized clinical trial

- Baseline measurements of daylong plasma glucose, insulin, and triglycerides in response to

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breakfast and lunch were obtained. For these measurements blood was drawn 9 times at hourly intervals. Lipid and lipoprotein measurements were also taken at baseline, including LDL-C, HDL-C,LDL-particle phenotype, LDL-cholesterol peak, and apolipoprotein B. These measurements were taken before breakfast when participants were fasting.

- Subjects were randomly assigned to a 16-week period of calorie restriction, during which they consumed one of two diets that were identical in protein (15% of total calories), saturated fat (7% of total calories), cholesterol (200 mg/day) and fiber (20 grams). The two diets varied in carbohydrate (40% vs 60%), monounsaturated and polyunsaturated fat (38% vs 18% of energy) and total fat (45% vs 25% of energy). Daily calorie requirements were calculated using the Harris-Benedict equation and an activity factor. Meals plans for each individual were developed based on a 750 calorie per day deficit. Subjects prepared their own food and kept detailed food records after receiving nutrition education on use of the American Diabetes Exchange lists for meal planning. Compliance was measured using food records and nutrition analysis of those records during weekly follow up visits.
- After a 16-week calorie restriction, a 2-week period of weight maintenance was initiated. At the end of this period all baseline measurements were repeated. Daylong measurements of plasma glucose and insulin were made in response to the experimental diet, not after the two-week weight maintenance period.

Blinding used (if applicable) implied with measurements

Intervention (if applicable):

Calorie-restricted diet containing either 60% of energy as carbohydrate and or 25% of energy as fat or 40% of energy as carbohydrate or 45% of energy as fat.

Statistical Analysis:

- Unpaired Student's *t* tests or chi-square tests were used to compare the two groups at baseline.
- Within-group changes in endpoints were assessed using paired Student's *t* tests.
- Between group differences in magnitude of change were compared using an analysis of covariance (ANCOVA).
- Evaluation of the potential for interaction between weight loss and diet with regard to improvement in insulin sensitivity was done using ANCOVA after adjusting for variables.

Data Collection Summary:

Timing of Measurements: Measurements were obtained at baseline and after 16 weeks of intervention and a 2-week period of weight maintenance.

Dependent Variables

- Daylong glucose as calculated by the trapezoidal method.
- Daylong insulin as calculated by the trapezoidal method
- Steady-state plasma glucose (SSPG) (insulin resistance) as calculated using the mean of blood insulin and glucose concentrations.
- Daylong triacylglycerol concentration as calculated by the trapezoidal method
- Total cholesterol as measured using the Vertical Auto Profile II method
- LDL-C as measured using the Vertical Auto Profile II method
- Narrow-density LDL-C as measured using the Vertical Auto Profile II method

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- Triglyceride as measured using the Vertical Auto Profile II method
- HDL-C as measured using the Vertical Auto Profile II method
- Apolipoprotein B as measured using International Reference Material
- LDL particle size as measured using LDL-cholesterol peak
- Intracellular Adhesion Molecule (ICAM) as measured using an enzyme-linked immunosorbent assay
- E-selectin as measured using an enzyme-linked immunosorbent assay.

Independent Variables:

- Hypocaloric diet containing 15% protein, 200 mg cholesterol, 20 grams, fiber, 40% carbohydrate, and 45% total fat.
- Hypocaloric diet containing 15% protein, 200 mg cholesterol, 20 grams fiber, 60% carbohydrate, and total 25% fat.

Control Variables

Description of Actual Data Sample:

Initial N: 65 (34 in the 60% carbohydrate diet and 31 in the 40% carbohydrate diet). Gender breakdown of the initial n was not provided.

Attrition (final N):8 persons did not complete the study (4 in each study group), making the final n= 57 (30 in the 60% carbohydrate group and 27 in the 40% carbohydrate group). Of those who completed the study, 39% were males and 61 percent females in the 60% carbohydrate group and 46 percent were males and 54 percent females in the 40% carbohydrate group.

Age: Mean age was 53±10 for the 60% carbohydrate group and 48±11 for the 40% carbohydrate group.

Ethnicity:The majority of the participants were white (80% in the 60% carbohydrate group and 88 percent in the 40% carbohydrate group). Other ethnic groups represented included Asians (10% of the 60% carbohydrate group and 4 percent of the 40% carbohydrate group) and Hispanics (10 percent of the 60% carbohydrate group and 8 percent of the 40% carbohydrate group).

Other relevant demographics: No information was provided on SES or education level of participants.

Anthropometrics: Weight in kg was similar between groups (94.3 kg ±14 and 95.0±10.9 for the 60% and 40% carbohydrate groups, respectively. BMI (kg/m² was 33±2.3 and 32.3±1.8 for the 60% carbohydrate and 40% carbohydrate groups, respectively.

Location: San Francisco Bay area, CA.

Summary of Results:

Key Findings:

- Patients lost weight in response to both dietary interventions (5.7±0.7 kg in the 60% carbohydrate group and 6.9±0.7kg in the 40% carbohydrate group). The difference in the amount of weight lost was not significant when the two diets were directly compared.

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- The SSPG concentration declined significantly overall, but the difference in the improvement in insulin sensitivity when the 2 diets were compared was not significant.
- There was no significant interaction between between the percentage weight loss and diet with respect to decrease in SSPG in the group as a whole.
- Irrespective of the diet, the more weight that was lost, the greater the magnitude of the decrease in SSPG concentration for all subjects combined.
- There was a greater decline in the along insulin for the group following the 40% carbohydrate diet compared to the 60% carbohydrate diet.
- Triacylglycerol concentrations decreased significantly only with the 40% carbohydrate diet.
- In many cases(daylong insulin concentrations, lipid and lipoprotein concentrations, and cellular adhesion molecules), changes in lipid and lipoprotein concentrations were noted, with greater decreases observed in the 40% carbohydrate versus the 60% carbohydrate diet.

Changes in weight and CVD risk factors in response to a hypocaloric diet containing 60% and 25% or 40% and 45% of energy as carbohydrate and fat, respectively.

Variable	60% Carbohydrate Diet	40% Carbohydrate Diet	Between Group Comparison	p value
	Before diet After Diet	Before diet After diet	Absolute difference(95% CI)	
Weight (kg)	94.3±14 88.6±14	95.0±10.9 88.2±9.9	-1.2(-8.3,8.5)	0.23
SSPG (mmol/L)	12.9±1.8 10.8±±2.4	13.7±2.6 10.6±3.7	-1.1(-2.6,0.4)	0.14
Systolic Blood pressure (mm Hg)	126±2 121±2	124±2 117±11	-2(-7,4)	0.30
Diastolic Blood Pressure (mm Hg)	74±9 72±9	76±7 73±7	0(-3,3)	0.70
Daylong glucose AUC	49.2±5.5 48.9±5.3	47.8±5.5 46.9±5.5	-0.67(-2.9,1.67)	0.31
mmol/L-8 h	866±99 880±95	860±97 844±99	-12(-163,81)	
mg/dL-8 h				
Daylong insulin AUC	3157±2935 2770±2569	3289±1700 2246±1234	-653(-1170,-129)	<0.01
pmol/L-8 h	440±409 386±358	458±237 313±172	-91 (-163,81)	
µU/mL-8 h				
Daylong triacylglycerol	19.5±8.7 18.1±9.0	23.1±13.1 16.6±7.4	-5.2(-1.2,9.2)	0.02
mmol/L-8 h	1731±769 1607±796	2047±1160 1471±658	460(102, 818)	
mg/dL-8 h				
Total cholesterol	5.2±1.0 4.9±1.0	4.7±0.9 4.9±1.0	0.46(0.06,0.86)	0.09
mmol/L	201±39 189±30	182±3.3 189±39	18(2,33)	
mg/dL				
LDL cholesterol	3.6±1.0 3.4±1.0	3.0±0.7 3.3±0.9	0.46(0.15, 0.82)	0.02
mmol/L	139±39 131±39	116±27 128±35	18(6,32)	
mg/dL				

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Narrow-density LDL-C mmol/L mg/dL	2.8±0.9 2.7±0.8 108±35 162±75	2.4±0.6 2.7±0.8 93±23 104±31	0.46(0.16,0.76) 18(6,29)	0.02
Triglyceride mmol/L mg/dL	1.9±0.8 1.8±0.9 168±74 165±75	2.2±1.3 1.7±0.9 199±146 146±77	-0.53(-0.95,-0.11) -47(-84,-10)	0.04
HDL cholesterol mmol/L mg/dL	1.06±0.21 1.03±0.23 41±8 40± 9	0.98±0.23 1.06±0.26 38±9 41±10	0.12(0.04,0.19) 5(2,7)	<0.01
Non HDL cholesterol mmol/L mg/dL	4.1±1.0 3.9±1.0 159±39 151±39	3.7±0.9 3.8±0.9 143±35 147±35	0.34(-0.14,0.72) 13(-5,28)	0.21
Apolipoprotein B mmol/L mg/dL	2.8±0.7 2,7±0.6 108±27 104±23	2.6±0.7 2.6±0.5 101±27 101±19	0.02(-0.22,0.25) 1(-9,to 10)	0.68
LDL size	116±6 116±5	114±6 117±5	1.82(0.22,3.43)	0.04
ICAM-1 ng/mL	650±34 596±26	652±40 558±20	-40.6(-1.08,27)	0.07
VCAM-1 ng/mL	856±33 857±28	895±40 891±41	-4.1(-61,52)	0.91
E-selectin ng/mL	114±10 92±8	94±10 67±4	-5.6(-25,14)	0.02

Actual composition on macronutrients consumed by subjects assigned to a diet with 60% and 25% or 40% and 45% of energy as carbohydrate and fat, respectively

	60% carbohydrate n=30	40% carbohydrate n=27	p
Carbohydrate	57±4%	41±4%	<0.00001
Protein	18±2%	18±2%	0.70
Total Fat	25±4	41±4	<0.00001
Saturated Fat	9±2	8±2	0.14
Poly or Monounsaturated fat	16±3	33±4	<0.0001

Other Findings:

- Both systolic and diastolic blood pressures were significantly lower for the two groups combined. The magnitude of the decreases in blood pressure did not vary as a function of the diet consumed.

Author Conclusion:

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In obese, insulin-resistant persons, a calorie-restricted diet, moderately lower in carbohydrate and higher in unsaturated fat, is as efficacious as the traditional low-fat diet in producing weight loss and may be more beneficial in reducing markers for cardiovascular disease risk.

Reviewer Comments:

- *It was not noted whether subjects were excluded if they were taking medications or nutrition supplements that might affect blood lipid levels.*
- *There was no discussion of the physical activity level of participants. Level of activity could affect amount of weight lost, blood pressure, blood lipids, and insulin resistance*
- *Classification into groups was done randomly but the method of randomizing subjects was not described.*
- *There was no discussion of why 8 participants dropped out of the study*
- *Diet period lasted only 16 weeks*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes

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2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	No
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	No
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	???
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	No

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5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes

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8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**		Yes
	8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
	8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
	8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
	8.6.	Was clinical significance as well as statistical significance reported?	Yes
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	Yes
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**		Yes
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes

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